

Exhibit A

(Part 1)

ISSUE CLASSIFICATION	
Class	Subclass

PATENT NUMBER

O.I.P.E.	PATENT DATE
SCANNED <u>4</u> <u>5/1</u> Q.A. <u>5/1</u>	

CLASS 250	SUBCLASS 1	ART UNIT 2981	EXAMINER XXX [Signature]
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APPLICANT(S):

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<input type="checkbox"/> TERMINAL DISCLAIMER	DRAWINGS		CLAIMS ALLOWED	
	Sheets Drwg.	Figs. Drwg	Print Fig.	Total Claims
<input type="checkbox"/> The term of this patent subsequent to _____ (date) has been disclaimed	_____ (Assistant Examiner) (Date)		NOTICE OF ALLOWANCE MAILED	
	<input type="checkbox"/> The term of this patent shall not extend beyond the expiration date of U.S Patent No. _____ _____		ISSUE FEE	
	_____ (Primary Examiner) (Date)		Amount Due	Date Paid
<input type="checkbox"/> The terminal _____ months of this patent have been disclaimed.	_____ (Legal Instruments Examiner) (Date)		ISSUE BATCH NUMBER	
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T005769

PATENT APPLICATION



09454273

JCS18 U.S. PTO
09/454273
12/03/99INITIALS Mjn

CONTENTS

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INTERFERENCE SEARCHED			
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SEARCH NOTES (INCLUDING SEARCH STRATEGY)		
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POSITION	INITIALS	ID NO.	DATE
FEE DETERMINATION	<i>MS</i>	<i>109804</i>	<i>12/15</i>
O.I.P.E. CLASSIFIER	<i>MTW</i>	<i>59</i>	<i>12-29-99</i>
FORMALITY REVIEW	<i>DW</i>	<i>72346</i>	<i>1-6-00</i>
RESPONSE FORMALITY REVIEW			

INDEX OF CLAIMS

✓ Rejected N Non-elected
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 + Restricted O Objected

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U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FEE RECORD SHEET

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U.S. GPO 1998-433-714/0045a

SERIAL NUMBER 09/454,273	FILING DATE 12/03/99	CLASS 25d	GROUP ART UNIT 2876	ATTORNEY DOCKET NO. A-67824/AJT
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APPLICANT

CONTINUING DOMESTIC DATA***
VERIFIED

371 (NAT'L STAGE) DATA***
VERIFIED

FOREIGN APPLICATIONS***
VERIFIED

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Foreign Priority claimed 35 USC 119 (a-d) conditions met	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> yes <input type="checkbox"/> no	Met after Allowance	STATE OR COUNTRY CA	SHEETS DRAWING 8	TOTAL CLAIMS 9	INDEPENDENT CLAIMS 4
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Verified and Acknowledged Examiner's Initials Initials

ADDRESS
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TITLE
MASS SPECTROMETER SYSTEM INCLUDING A DOUBLE ION GUIDE INTERFACE AND METHOD OF OPERATION

FILING FEE RECEIVED \$1,098	<p><i>8 sheets of formal Drawings filed 1/14/01</i></p> <p>FEES: Authority has been given in Paper</p> <p>No. _____ to charge/credit DEPOSIT ACCOUNT</p> <p>NO. _____ for the following:</p>	<input type="checkbox"/> All Fees <input type="checkbox"/> 1.18 Fees (Filing) <input type="checkbox"/> 1.17 Fees (Processing Ext. of time) <input type="checkbox"/> 1.18 Fees (Issue) <input type="checkbox"/> Other _____ <input type="checkbox"/> Credit
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5 Field of the Invention

Background of the Invention

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and the mass analyzer which is operated at vacuum pressures in the free molecular flow region.

The prior art interface vacuum stages have included ion guides to transfer the ions through the stages of decreasing pressure into the mass analyzer. In many prior art systems, the ions are guided by electrostatic lenses. In other systems, the ions are guided by electrodynamic multipole ion guides.

The use of an r.f.-only octopole ion guide for focusing and guiding ion beams has been described by Teloy and Gerlich (Chem. Phys., Vol. 4, p. 417, 1974) and Jarrold et. al. (Mol. Phys., Vol. 39, p. 787, 1980).

10 The dissociation of mass-selected ions in an r.f.-only quadrupole by collision with a target gas at low translational energies ($E_{lab} < \text{about } 100 \text{ eV}$) has been described by R. A. Yost and C. G. Enke et. al. (Anal. Chem., Vol. 51, p. 1251a, 1979), and Dawson et. al. (Int. J. Mass Spec. Ion Proc., Vol. 42, p. 195, 1982).

McIver et. al. described the use of an r.f.-only quadrupole ion guide for guiding a beam of mass-selected ions into a Fourier-transform ion cyclotron resonance mass analyzer (Int. J. Mass Spec. Ion Proc., Vol. 64, p. 67, 1985).

Szabo described the theory of operation for multipole ion guides with various electrode structures (Int. J. Mass Spec. Ion Proc., Vol. 73, pp. 197-312, 1986).

Efficient transport of ions through vacuum chambers by multipole ion guides has been described by Smith et. al. (Anal. Chem., Vol. 60, pp. 436-441, 1988).

Beu et. al. described the use of three quadrupole ion guides to transport ions from an atmospheric pressure ionization source through three vacuum pumping stages into a Fourier-transform ion cyclotron resonance mass analyzer (J. Am. Soc. Mass Spec., Vol. 4, pp. 557-565, 1993).

25 U.S. Patent No. 4,963,736 describes the use of a multipole ion guide in the first pumping stage of a two-stage system. Operation of the multipole ion guide in certain length-times-pressure regimes is claimed for the purposes of enhancing ion signal.

U.S. Patent No's. 5,179,278 and 5,811,800 describe the temporary storage of ions in an rf multipole rod system for subsequent analysis in an r.f. quadrupole ion trap mass spectrometer. This is done for the purpose of matching the time scales of

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compounds eluting from chromatographic or electrophoretic separation devices to the time scale of mass spectrometric analyses performed by an r.f. quadrupole ion trap.

U.S. Patent No. 5,432,343 describes an ion focusing lensing system for interfacing an atmospheric pressure ionization source to a mass spectrometer. It describes the use of an electrostatic lens in a transition flow pressure region of the interface, claiming benefit of independent adjustment of operating voltages controlling the collisionally induced dissociation and declustering processes. Enhancement of ion beam transmission into the mass analyzer is also claimed.

U.S. Patent No. 5,652,427 describes in one embodiment a system in which a multipole ion guide extends between two vacuum stages and in another embodiment a system which includes a multipole in each of two adjacent stages. Improved performance and lower cost are claimed.

U.S. Patent No. 5,852,294 describes the construction of a miniature multipole ion guide assembly.

A goal to be achieved in all single or multiple interface vacuum chambers is to transport as many protonated molecular cations or molecular anions as possible from the atmospheric pressure ionization source to the mass analyzer. However, many solvent adduct ions which are formed in the high pressure region travel through the interface vacuum chambers into the analyzer. The process of solvent adduction in the mass spectrometer system is generally considered to be a non-covalent association between sample ions of interest and neutral solvent molecules. Thus, in the case of introduction of an analyte into an electrospray or atmospheric pressure chemical ionization source, the ion current produced from that analyte may be divided between the protonated molecular cation or molecular anion and one or more solvent adduct species. Specific detection is usually accomplished by monitoring the ion signal, or derivative of that signal, for one specific mass. In the case where solvent adducts are formed, the limit of detection or limit of quantitation for the analyte is reduced.

Experimental evidence indicates that these adduct ions are predominantly formed in the high pressure regions of the system ranging from the API source region through the interface vacuum regions. The degree of adduction varies directly with the pressures in these regions. The formation of adduct ions significantly reduces the

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abundance of sample analyte ions. Furthermore, the adduct ions which enter into the mass analyzer complicates the mass spectrum and make the identification of mass peaks more difficult.

5 Objects and Summary of the Invention

It is an object of the present invention to provide a mass spectrometer system employing an ion source with multiple ion guides configured and operated to convert adduct ions into sample ions and a method of operating multiple ion guides to convert adduct ions into sample ions to thereby increase the analyte ions current and sensitivity

10 of the mass spectrometer system.

In accordance with the invention, there is provided a mass spectrometer including a mass analyzer disposed in a high vacuum chamber for analyzing ions formed in an ionization source which includes first and second evacuated interface chambers immediately preceding the mass analyzer chamber, with the first interface
 15 chamber being at a higher pressure than the second interface chamber, and including a first ion guide for guiding ions from the ion source into said second interface chamber which includes a second multipole ion guide for guiding the ions from the first interface chamber into the high vacuum analyzer chamber for analysis. Both r.f. and DC potentials are applied to the said first and second ion guides to ensure ion focusing
 20 and transmission through related vacuum chamber. A first ion lens is disposed at the input of the first interface chamber for directing ions into the first multipole ion guide, an interchamber ion lens is disposed between the first and second interface chambers for directing ions into said second multipole ion guide, and an ion lens or a lens stack is disposed between the second interface chamber and the analyzer chamber for
 25 directing ions into said analyzer for analysis. These ion lenses also serve as gas conductance restrictors between said interface chambers.

A DC voltage source is connected to provide a potential difference between the interchamber lens and the second multipole ion guide which defines the ion's translational kinetic energy as it enters the second interface chamber. The ion's kinetic
 30 energy is chosen such that at the vacuum pressure of the second interface chamber adduct ions are converted into sample ions by collision induced dissociation without

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fragmentation of sample ions whereby the sample ion current entering the analyzer is increased, thereby increasing the sensitivity of the mass spectrometer system.

There is provided a method of mass analyzing ions produced in an atmospheric pressure ionization source in which adduct ions formed in the mass spectrometer system are dissociated prior to analysis to increase the analyte ion current to the mass analyzer and the sensitivity of the mass spectrometer system.

There is provided a method of operating a mass spectrometer system in which an analyzer in a vacuum chamber analyzes ions formed in an atmospheric pressure ionization source. The system includes first and second multipole ion guides disposed in serial first and second evacuated chambers immediately preceding the analyzer. The method comprises applying a DC voltage between the ion lens and the second multipole ion guide which has an amplitude selected to dissociate any adduct ions at the pressure of the second chamber without fragmenting the sample ions whereby to increase the sample ion current directed into the analyzer and the sensitivity of the mass spectrometer system.

Brief Description of the Drawings

The foregoing and other objects of the invention will be more clearly understood from the following description when read in conjunction with the accompanying drawings in which:

Figure 1 is a schematic view of a mass spectrometer system including an atmospheric pressure ion source coupled to a tandem mass analyzer through evacuated interface chambers with multipole ion guides.

Figures 2A and 2B show the mass spectra for an injection of Alprazolam in a liquid stream flowing at 400 microliters per minute ($\mu\text{l}/\text{min}$) with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 3A and 3B show the mass spectra for an injection of Alprazolam in a liquid stream flowing at 1 milliliter per minute (ml/min) with -5V DC offset and -15V DC offset applied to the second ion guide.

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Figures 4A and 4B show the mass spectra for an injection of codeine-d3 in a liquid stream flowing at 400 μ l/min with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 5A and 5B show the mass spectra for an injection of codeine-d3 in a liquid stream flowing at 1 ml/min with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 6A and 6B show the mass spectra for an injection of acetaminophen in a liquid stream flowing at 400 μ l/min flow with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 7A and 7B show the mass spectra for an injection of Ibuprofen in a liquid stream flowing at 400 μ l/min with +5V DC offset and +15V DC offset applied to the second ion guide.

Figure 8 is a schematic view of a mass spectrometer system as in Figure 1 with a single quadrupole mass analyzer rather than a tandem mass analyzer or other suitable mass analyzer.

Description of Preferred Embodiments

Referring to Figure 1, an atmospheric pressure ion source in chamber 11 is interfaced to a tandem mass analyzer 12 via three vacuum pumping stages. The first stage 13 which has the highest pressure is evacuated by an oil-filled rotary vane vacuum pump 14. Other types of vacuum pumps may also be used for this stage, such as a diaphragm pump or scroll pump. A typical pressure for first stage 13 is between 1 and 2 Torr. The second and third stages 16 and 17 are separated by a lens 18 with an orifice 19, which in one example was 1.5 mm in diameter, and can be evacuated by a hybrid or compound turbomolecular pump 21 which includes both turbomolecular and molecular drag pumping stages, and may have multiple inlets into each of these pumping stages, or by individual vacuum pumps (not shown). As will be explained in accordance with the present invention, the pressure in chamber 16 is below 500 mTorr preferably below 250 mTorr, and more preferably below 175 mTorr; and the pressure in chamber 17 is below 1 mTorr, preferably below 0.7 mTorr, and more preferably

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below 0.5 mTorr. The pressure in the tandem mass analyzer chamber is approximately 1×10^{-5} Torr or below.

The atmospheric pressure ion source may be an electrospray ion source or atmospheric pressure chemical ionization source. With either ion source, sample liquid is introduced into the chamber 11, which is at atmospheric pressure, and ionized. The ions are drawn through a capillary 22, which may be heated, into chamber 13. The end of the capillary is opposite a conical skimmer 24 which includes a central orifice or aperture 26. The skimmer separates the low pressure stage 13 from the lower pressure stage 16. A portion of the ion and gas flow is skimmed from the free jet expansion leaving the capillary and enters the second lower pressure stage. The ions which travel through the skimmer are guided into the mass analyzer by first and second multipole ion guides 27 and 28. In one example, the ion guides are square quadrupoles. The guide 27 is 1.25 inches long and the guide 28 is 3.37 inches with the rods separated by 0.118 inches (3 mm). The ion guides are mounted coaxially using polycarbonate holders (not shown). The quadrupole ion guides are operated by applying AC voltages 31 and 32 to the poles which guide ions as is well known. Ions which enter the second and third stages drift under the influence of DC voltage 33 applied between the skimmer lens 24 and lens 18, and by DC voltage 34 applied between the lens 18 and the lens 36.

As discussed above, solvent adduct ions are formed in the high pressure regions ranging from the atmospheric pressure region to the quadrupole ion guide stages or regions. The degree of adduction is believed to vary directly with the pressure in these regions. The formation of adduct ions can significantly reduce the abundance of sample analyte ions which reach the analyzer. Consequently, effective conversion of the adduct ions into protonated molecular cations or molecular anions can greatly enhance the sample ion current and the sensitivity of the mass spectrometer system.

We have discovered that the solvent adduct ions can be dissociated and converted into sample ions in the second ion guide 28 by applying a small DC offset voltage between the ion guide 28 and the lens 18 to increase the energy of the solvent adduct ions. An additional 10 volts DC offset applied to the second ion guide (usually

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used with a standard 5 V DC offset) is sufficient to convert the solvent adducts into the protonated molecular cation or molecular anion for all compounds tested. In addition, this offset voltage is insufficient to cause fragmentation of the analyte ions at the pressure of the second stage.

Both pumping efficiency and solvent adduction were evaluated. The pumping requirement and vacuum condition on the double ion guide system were compared to a standard TSQ 7000 system sold by ThermoQuest Corporation under the same gas load conditions. Several different compounds including a) acetaminophen; b) Alprazolam; c) codeine-d3; d) ibuprofen were used to investigate the degree of solvent adduction, conversion to protonated molecular cation or molecular anion, and fragmentation of the protonated molecular cation or molecular anion. The solvent used in the experiment was 50:50 acetonitrile:water + 5mM ammonium acetate adjusted to a pH of 4.5. Table I lists the main experimental conditions, compound, molecular weight and type of solvent adduction investigated.

TABLE I

Compound	Molecular Weight	Solvent Adduct	Ion Polarity	LC Flow (μ l/min)	Sample Injected (ng)
Acetaminophen	151	Acetonitrile	Positive	400	500
Alprazolam	308	Acetonitrile	Positive	400 - 1000	1.6
Codeine-d3	302	Acetonitrile	Positive	400 - 1000	50
Ibuprofen	206	Acetate	Negative	200	50

Figures 2-7 show the comparative mass spectra for the four different compounds used in the evaluation under standard (± 5 V DC) offset and an incremental 10 V DC (± 15 V DC total) offset conditions between the interstage ion lens 18 and the second multipole ion guide 28 indicating that the signal intensity and peak area for the protonated molecular cations or molecular anions can be significantly enhanced by the application of the increased DC offset on the second multipole ion guide 28.

Figure 2A shows the mass scan for Alprazolam at 400 μ l/min liquid chromatograph flow with the standard -5 volt offset, and Figure 2B shows Alprazolam

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with an incremental 10 volts of offset at the same flow rate. The increased sample ion signal produced by the incremental offset voltage is apparent.

Figures 3A and 3B show the mass spectra for Alprazolam at 1 ml/min flow. Again the increased sample ion current is apparent. Figures 4A and 4B show the mass spectra for codeine-d3 at 400 μ l/min flow with the standard and increased offset voltages. The increased sample ion signal at m/z 302 is apparent. The same mass spectra are shown for 1 ml/min codeine-d3 in Figures 5A and 5B. Figures 6A and 6B show a comparison of the mass spectra for Acetaminophen at 400 μ l/min flow with the standard and increased offset voltages. Again, the vast improvement in sensitivity is apparent. Figures 7A and 7B show the mass spectra for ibuprofen flowing at 400 μ l/min flow with the standard and increased offset voltages. The improved signal at m/z 205 should be noted.

The DC offset required for high efficiency solvent adduct ion conversion at different vacuum conditions in both first chamber and second chamber was also investigated. The following tables summarize one set of tests in which the ratio of the acetonitrile adduct to the protonated molecular cation of codeine-d3 was investigated at different pressures and different DC offset voltages on the second ion guide.

TABLE 2

DC offset on second ion guide (volts)	-5	-5	-5	-5	-5
First ion guide pressure (mTorr)	609	563	502	224	167
Second ion guide pressure (mTorr)	1.6	1.2	1	0.7	0.5
Ratio of acetonitrile adduct ion to protonated molecular ion	704%	926%	288%	354%	248%

DC offset on second ion guide (volts)	-15	-15	-15	-15	-15
First ion guide pressure (mTorr)	609	563	502	224	167
Second ion guide pressure (mTorr)	1.6	1.2	1	0.7	0.5
Ratio of acetonitrile adduct ion to protonated molecular ion	445%	407%	82%	38%	17%

DC offset on second ion guide (volts)	-35	-35	-35	-35	-35
First ion guide pressure (mTorr)	609	563	502	224	167

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Second ion guide pressure (mTorr)	1.6	1.2	1	0.7	0.5
Ratio of acetonitrile adduct ion to protonated molecular ion	300%	248%	40%	7%	3%

The bold data in Table 2 indicates the range of pressure and offset voltages at which the most efficient conversion of solvent adduct to protonated molecular cation is achieved. According to these results, the operating pressure for the ion guides should be:

First Ion Guide: below 500 mTorr

Second Ion Guide: below 1 mTorr

The DC offset voltage range for efficient solvent adduction conversion should be ± 10 to ± 30 Volts, although ± 10 V is preferable.

The preferred pressure range is less than 250 mTorr for the first stage and 0.7 mTorr for the second stage, and the most preferred pressure range is less than 175 mTorr for the first stage, and 0.5 mTorr for the second stage.

The present invention can be used for other types of mass analyzers such as quadrupole mass analyzers of the type described in U.S. Patent Nos. 4,540,884 and RE 34,000. Figure 8 shows the interface stages and ion guides associated with a quadrupole mass analyzer 41 disposed in the vacuum chamber 12. Like members have been applied to the parts which correspond to those in Figure 1. It is apparent that the invention is applicable to other types of mass analyzers such as quadrupole ion trap, ion cyclotron resonance (i.e., magnetic ion trap), time-of-flight, magnetic sector, and double-focusing magnetic/electric sector, monopole, etc.

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What is Claimed is:

1. A mass spectrometer system including a mass analyzer disposed in a high vacuum chamber for analyzing ions formed at atmospheric pressure and directed to the analyzer through intermediate vacuum chambers including:

- 5 first and second evacuated chambers directly preceding the mass analyzer chamber with the first chamber being at a higher pressure than the second chamber,
 a first multipole ion guide in the first chamber for guiding ions into said second chamber,
 a second multipole ion guide in the second chamber for guiding ions from the
 10 first chamber into the high vacuum chamber for mass analysis,
 an interchamber ion lens between the first and second chambers, and
 a DC voltage source connected between said interchamber lens and said second multipole ion guide for applying a voltage therebetween having an amplitude that at
 the vacuum pressure of the second interface chamber adduct ions traveling into the
 15 chamber are converted into protonated molecular cations or molecular anions ions without fragmentation of these ions whereby to increase the sample ion current and therefore the sensitivity of the mass spectrometer system.

2. A method of mass analyzing ions produced at atmospheric pressure, in
 20 which adduct ions are formed, and introduced into a mass analyzer disposed in a vacuum chamber,
 the step of dissociating the adduct ions to increase the analyte ion current into the mass analyzer.

- 25 3. The method of operating a mass spectrometer system including a mass analyzer which analyzes ions formed at atmospheric pressure, said system including
 first and second multipole ion guides disposed in serial first and second evacuated chambers separated by an ion lens for guiding analyte ions into said mass analyzer, which comprises
 30 applying a DC voltage between the ion lens and the second multipole ion guide having an amplitude selected to dissociate adduct ions at the pressure of the second

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chamber to increase the sample ion current and the sensitivity of the mass spectrometer system.

4. A mass spectrometer system including a mass analyzer disposed in a high vacuum chamber for analyzing ions formed at pressures substantially near atmospheric pressure and directed to the analyzer through intermediate vacuum chambers including:

- first and second evacuated chambers directly preceding the mass analyzer chamber with the first chamber being at a higher pressure than the second chamber,
- 10 a first multipole ion guide in the first interface chamber for guiding ions into said second interface chamber,
- a second multipole ion guide in the second chamber for guiding ions from the first chamber into the high vacuum analyzer chamber for analysis,
- an interchamber ion lens between the first and second interface chambers, and
- 15 a DC voltage source connected between the interchamber lens and the second multipole ion guide for applying a voltage therebetween having an amplitude that at the vacuum pressure of the second interface chamber adduct ions traveling into the chamber are converted into sample ions without fragmentation of sample ions whereby to increase the sample ion current and therefore the sensitivity of the mass
- 20 spectrometer system.

5. A mass spectrometer system as in claim 4 in which the pressure in the first chamber is below 500 mTorr, and in the second chamber is below 1 mTorr, and the offset voltage applied between the interchamber lens and the second multipole ion
- 25 guide is between ± 10 volts and ± 30 volts.

6. A mass spectrometer system as in claim 5 in which the pressure in the first chamber is less than 250 mTorr, and in the second chamber is less than 0.7 mTorr.

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7. A mass spectrometer system as in claim 5 in which the pressure in the first chamber is less than 175 mTorr, and in the second chamber is less than 0.5 mTorr.

5 8. A mass spectrometer as in claim 6 or 7 in which the offset voltage is ± 10 volts.

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DECLARATION FOR PATENT APPLICATION

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled MASS SPECTROMETER SYSTEM INCLUDING A DOUBLE ION GUIDE INTERFACE AND METHOD OF OPERATION.

the specification of which

(check one) ☒ is attached hereto.
☐ was filed on _____ as
 Application Serial No. _____
 and was amended on _____
 (if applicable)

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Patent Office all information known to me to be material to patentability as defined in 37 C.F.R. 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed

Prior Foreign Application(s)			Priority Claimed	
_____ (Number)	_____ (Country)	_____ (Day/Month/Year Filed)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____ (Number)	_____ (Country)	_____ (Day/Month/Year Filed)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____ (Number)	_____ (Country)	_____ (Day/Month/Year Filed)	<input type="checkbox"/> Yes	<input type="checkbox"/> No

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112. I acknowledge the duty to disclose to the Patent Office all information known to me to be material to patentability as defined in 37 C.F.R. 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.)	(Filing Date)	(Status)
_____	_____	(patented, pending, abandoned)

Direct all telephone calls to Aldo J. Test at (650) 494-8700.

Address all correspondence to: Aldo J. Test
FLEHR HOBBACH TEST
ALBRITTON & HERBERT LLP
Suite 3400, Four Embarcadero Center
San Francisco, California 94111

File No. A-67824/AJT

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Title 18, United States Code, §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of

first inventor: Kegj Tang

Inventor's signature: [Signature]

Date: 11/30/99

Residence: Cupertino, California

Citizenship: PRC

Post Office Address: 10302 Terry Way, #1, Cupertino, CA 95014

Full name of

second inventor: Alan E. Schoen

Inventor's signature: [Signature]

Date: Nov 30, 1999

Residence: Saratoga, California

Citizenship: US

Post Office Address: 16810 Eohlman Road, Saratoga, California 95070

Full name of

third inventor: Jean-Jacques Danyach

Inventor's signature: [Signature]

Date: 11/30/99

Residence: San Jose, California

Citizenship: French

Post Office Address: 373 River Oaks Circle, #2010, San Jose, CA 95134

A-67824/AJT

DECLARATION FOR PATENT APPLICATION
Page 2

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POWER OF ATTORNEY BY ASSIGNEE

(Accompanying Application)

The undersigned assignee of the entire interest in application for letters patent entitled: MASS SPECTROMETER SYSTEM INCLUDING A DOUBLE ION GUIDE INTERFACE AND METHOD OF OPERATION, and having the named inventors: Keqi Tang, Alan E. Schoen and Jean-Jacques Duryach, hereby appoints the following attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith; said appointment to be to the exclusion of the inventor(s) and his (their) attorney(s) in accordance with the provisions of 37 C.F.R. 3.71: Harold C. Hohbach, Reg. No. 17,757; Aldo J. Test, Reg. No. 18,048; Thomas O. Herbert, Reg. No. 18,612; Donald N. Macintosh, Reg. No. 20,316; Edward S. Wright, Reg. No. 24,903; David J. Brezner, Reg. No. 24,774; Richard E. Backus, Reg. No. 22,701; James A. Sheridan, Reg. No. 25,436; Robert B. Chickering, Reg. No. 24,286; Richard F. Trecartin, Reg. No. 31,801; Steven F. Caserza, Reg. No. 29,780; Laura L. Kulhanjian, Reg. No. 33,257; Michael A. Kaufman, Reg. No. 32,988; Janet E. Muller, Reg. No. 35,294; Edward N. Bachand, Reg. No. 37,085; R. Michael Ananian, Reg. No. 35,050; Stephen M. Knauer, Reg. No. 38,208; Robin M. Silva, Reg. No. 38,304; David C. Ashby, Reg. No. 36,432; Julian Caplan, Reg. No. 14,785; Maria S. Swiatek, Reg. No. 37,244; provided that if any one of said attorneys ceases being affiliated with the law firm of Flehr Hohbach Test Albritton & Herbert LLP as partner, employee or of counsel, such attorney's appointment as attorney and all powers derived therefrom shall terminate on the date such attorney ceases being so affiliated.

In accordance with 37 CFR 3.73 the assignee hereby certifies that the evidentiary documents with respect to its ownership have been reviewed and that, to the best of assignee's knowledge and belief, title is in the assignee seeking to take this action.

Direct all telephone calls to Aldo J. Test at (650) 494-8700.

Address all correspondence to:

Aldo J. Test
FLEHR HOHBACH TEST
ALBRITTON & HERBERT LLP
Suite 3400, Four Embarcadero Center
San Francisco, California 94111-4187

Date: November 30, 1999

Assignee: FINNIGAN CORPORATION

By: [Signature]

Print: JEAN JARDINE

Title: President, Finnigan Corporation

355 River Oaks Parkway
San Jose, CA 95134

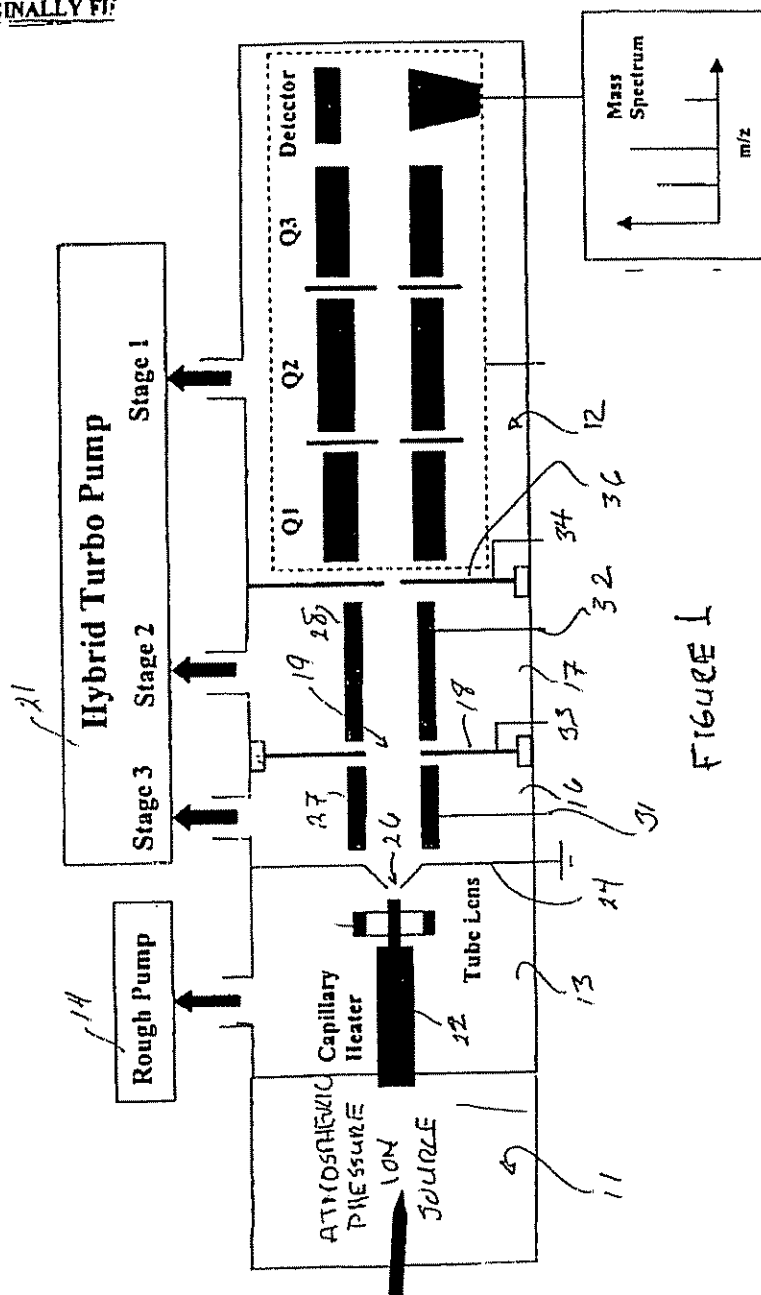
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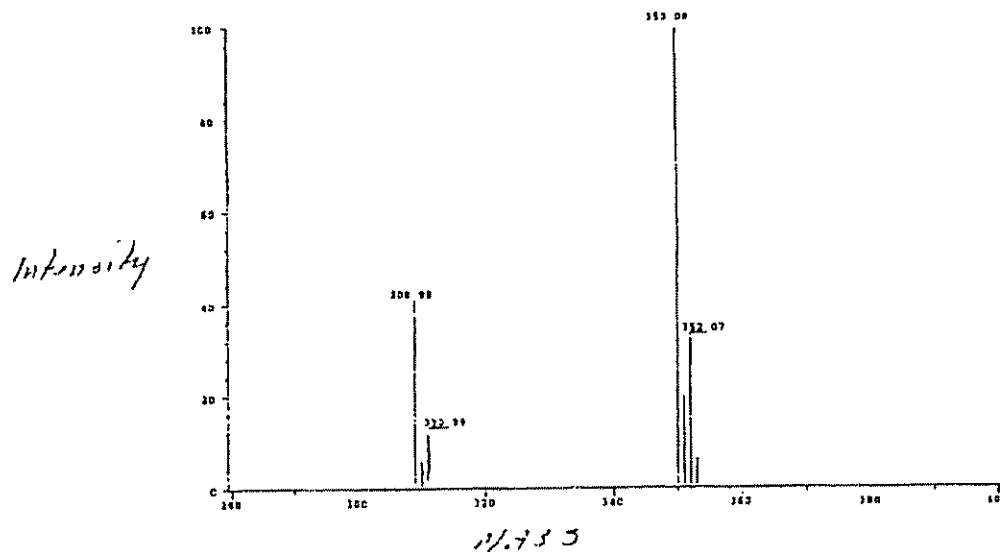


FIGURE 2A

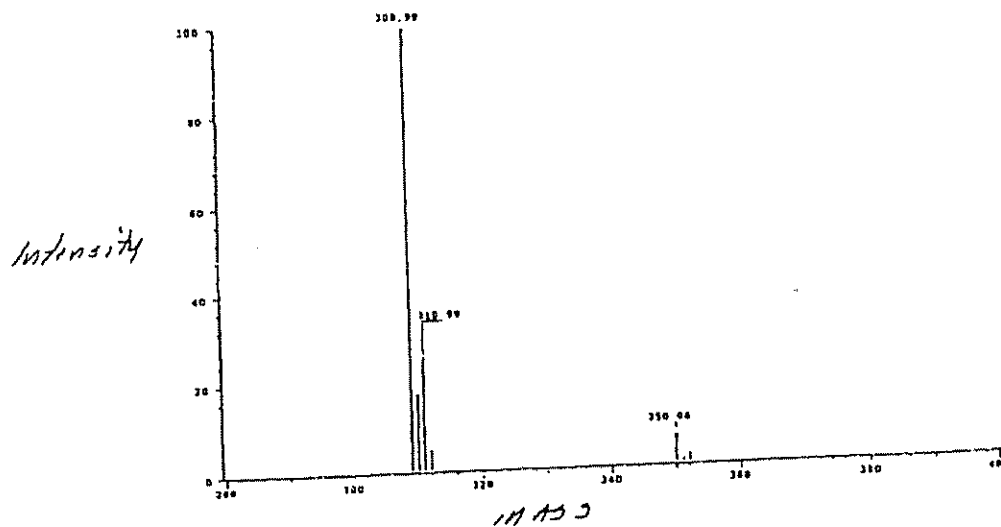
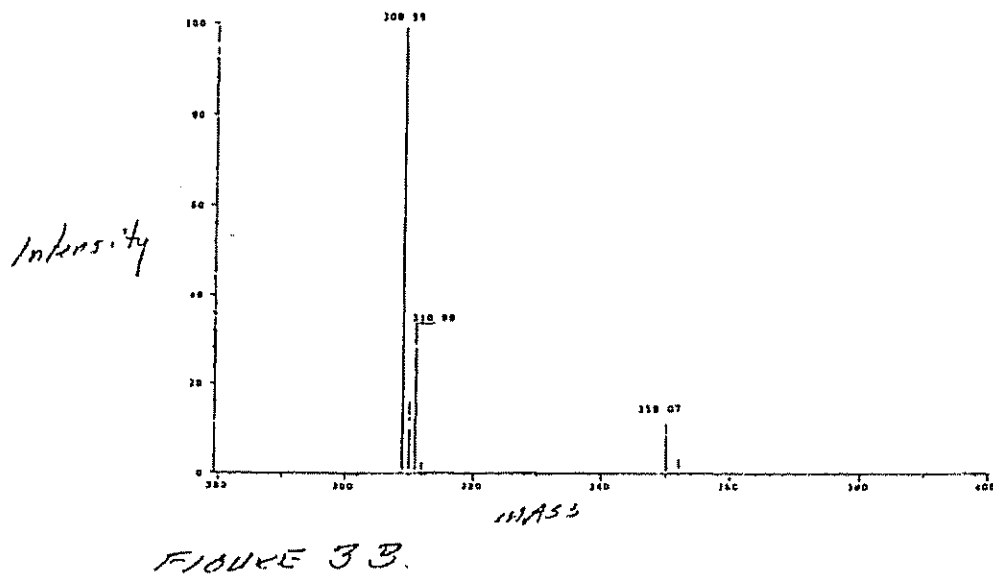
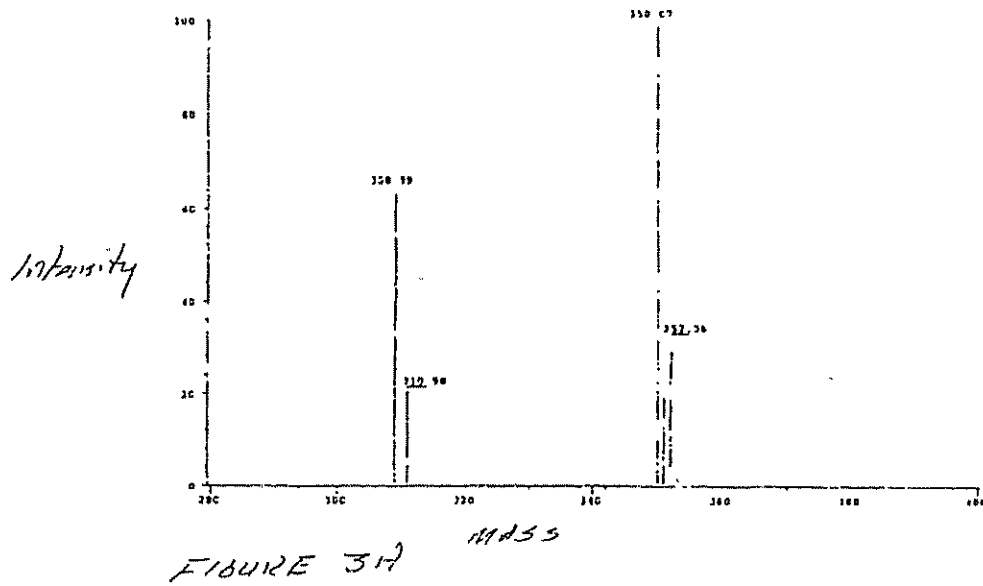


FIGURE 2B

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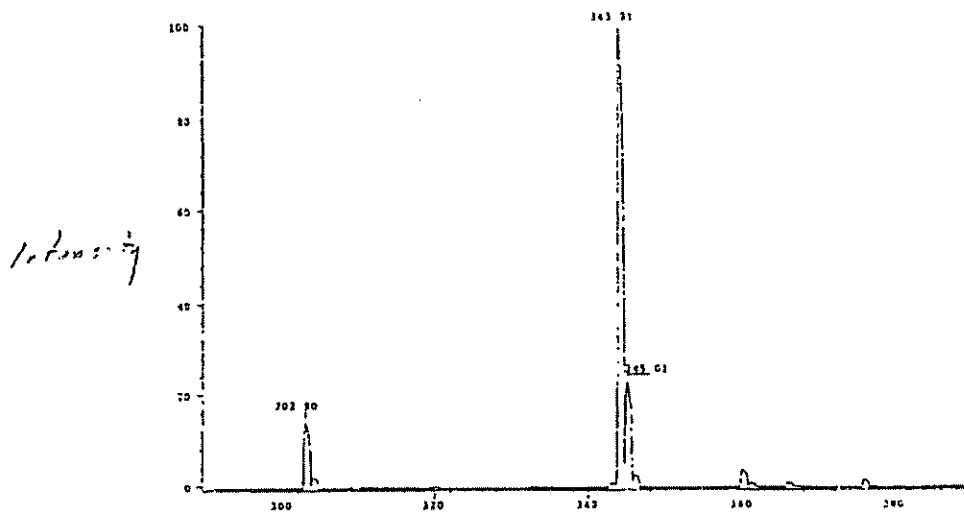


FIGURE 11A

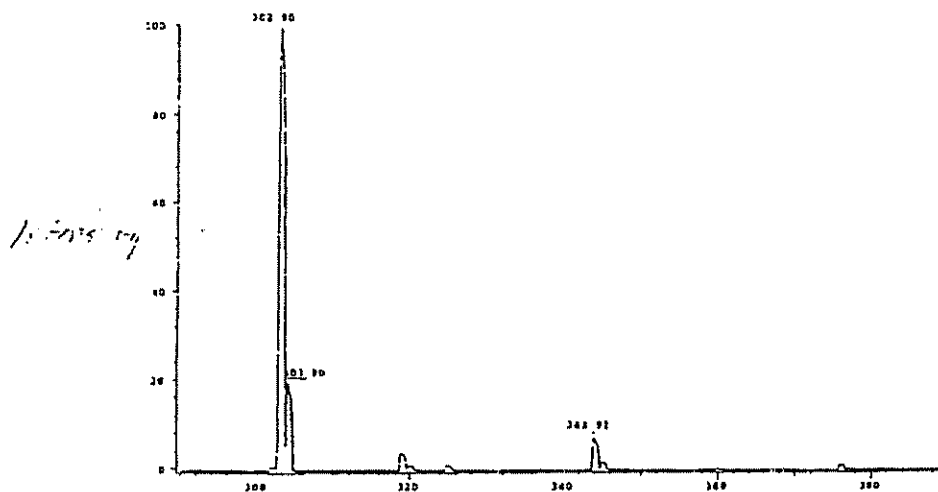
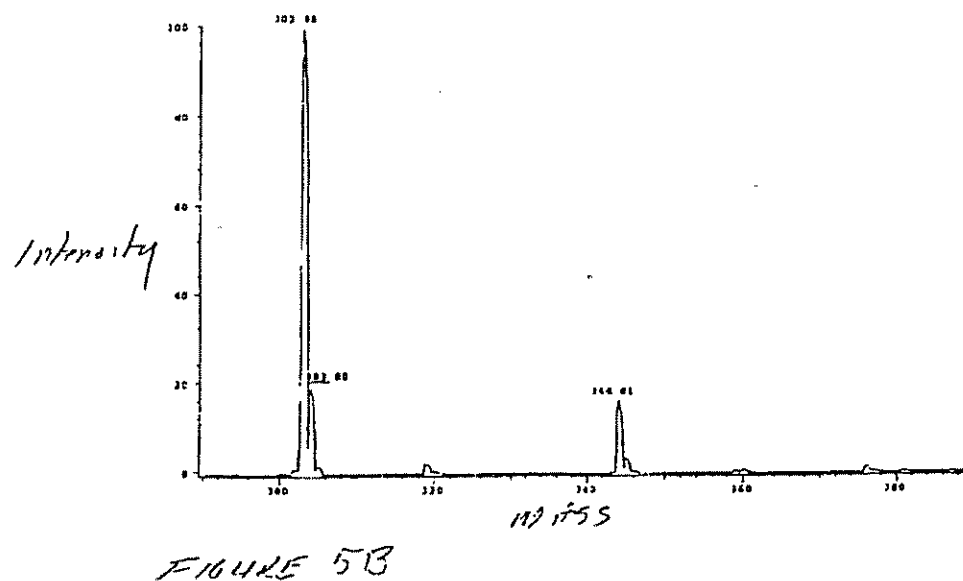
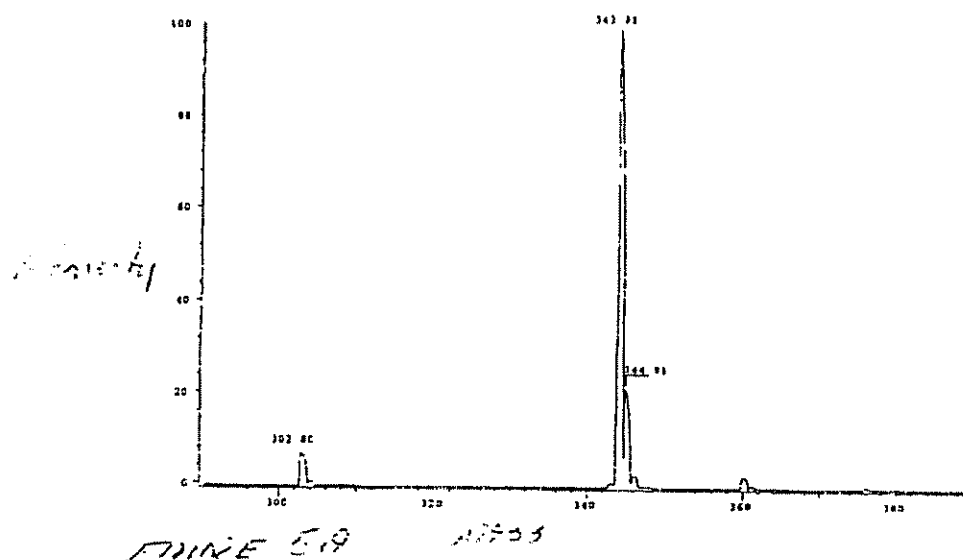


FIGURE 11B

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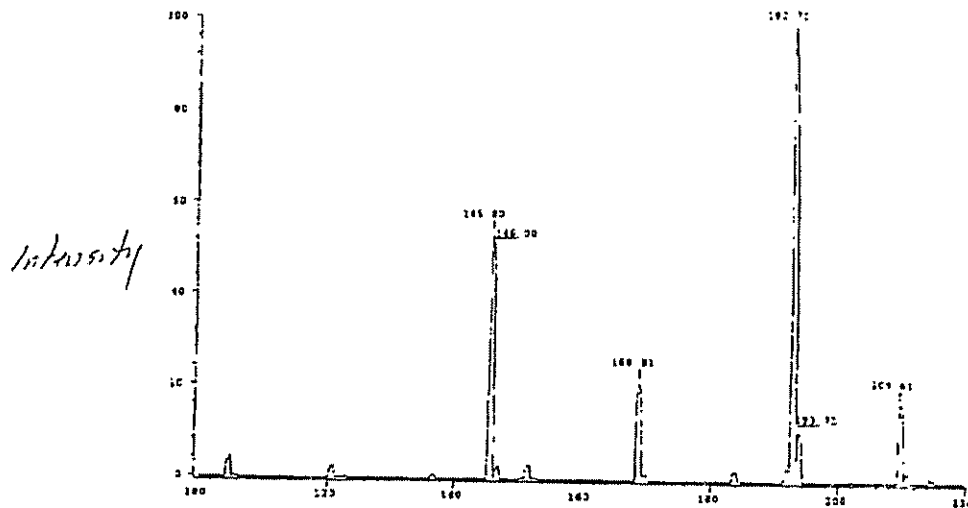


FIGURE 6A

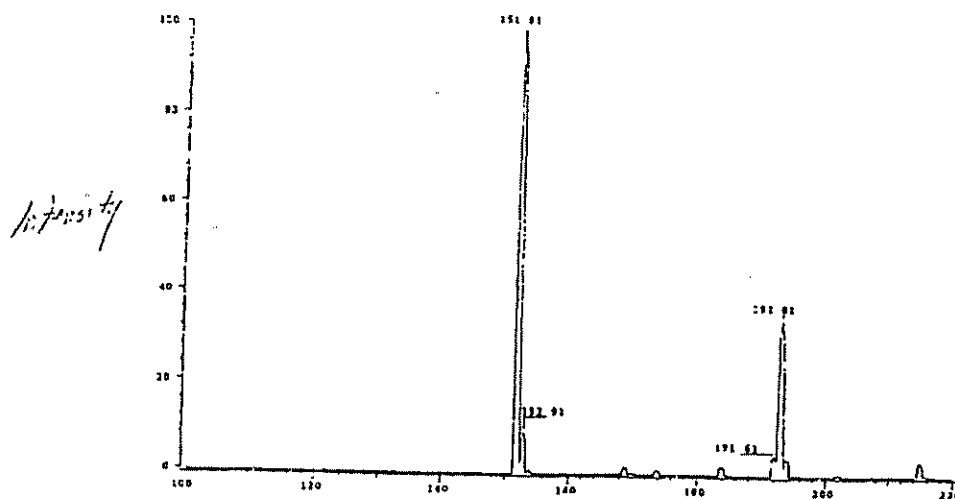
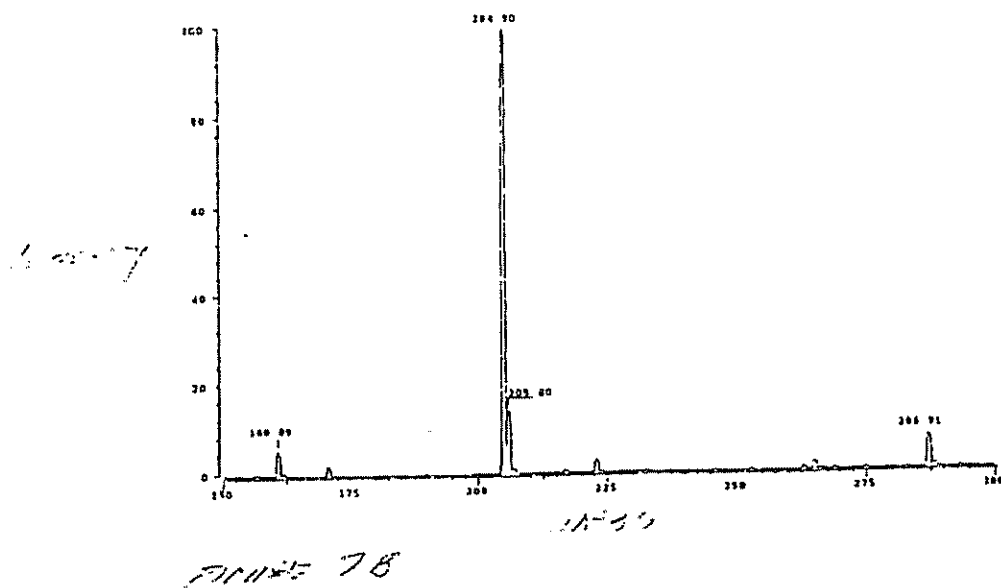
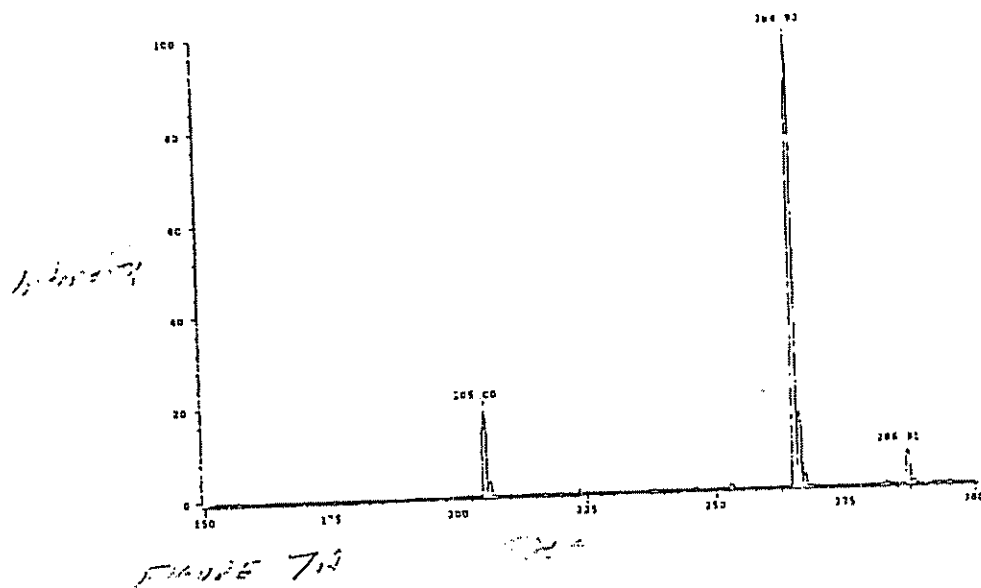
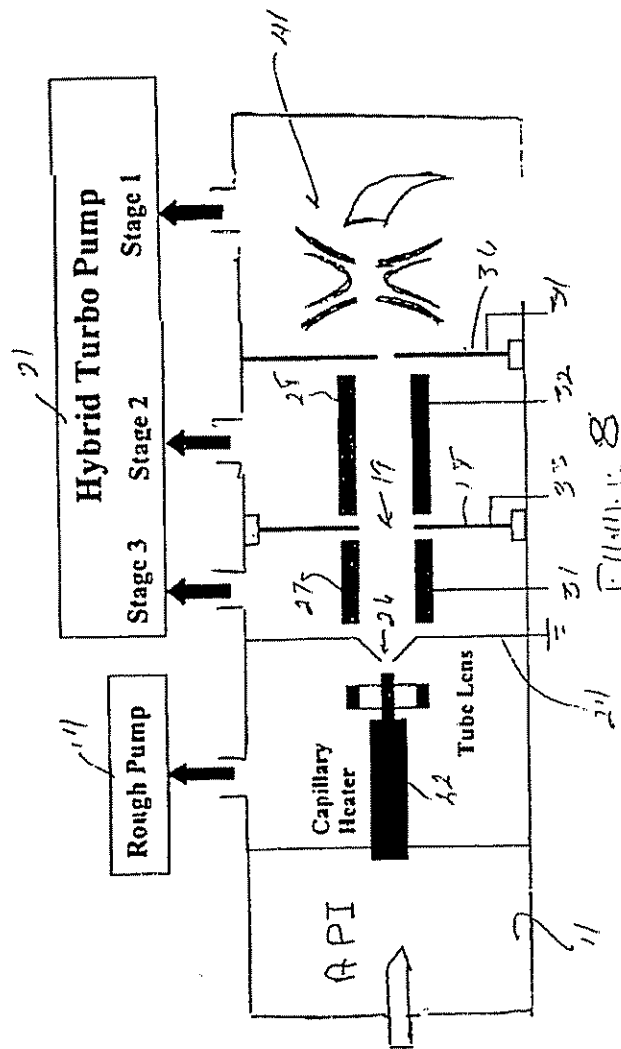


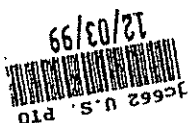
FIGURE 6B

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INDICATED ABOVE AND IS ADDRESSED TO: BOX PATENT APPLICATION
FEE ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON,
20231TYPED NAME KARI BATEMANSIGNED Kari Bateman

Sir:

Transmitted herewith for filing is the patent application of Inventor(s): Keqi Tang, Alan E. Schoon, Jean-
Jacques DuniachFor: MASS SPECTROMETER SYSTEM INCLUDING A DOUBLE ION GUIDE INTERFACE AND METHOD OF
OPERATION

Enclosed are also:

- ☒ Prior Art Statement
☒ 8 Sheets of drawing, Formal ☐ Informal ☒
☒ An Assignment of the invention to: Finnigan Corporation
☒ Power of Attorney by Assignee & Exclusion of Inventor Under 37 CFR 3.71
☒ Declaration for Patent Application

	(Col. 1) NO. FILED	(Col. 2) NO. EXTRA	SMALL ENTITY RATE	FEE	OTHER THAN SMALL ENTITY RATE	FEE
BASIC FEE				\$380		\$760
TOTAL CLAIMS	9 - 20 = 0	0	x 9 =	\$	x 18 =	\$
INDEP CLAIMS	4 - 3 = 0	1	x 39 =	\$	x 78 =	\$78
MULTIPLE DEPENDENT CLAIM PRESENTED			+130 =	\$	+260 =	\$260
If the difference in Col. 1 is less than zero, enter '0' in Col. 2			TOTAL	\$	TOTAL	\$1098.00

☒ Our Check in the amount of \$1138.00 (\$1098 to cover the filing fee and \$40 to cover the cost of assignment recordation) is enclosed.

- ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, including extension fees, or credit any overpayment to Deposit Account No. 06-1300 (Order No. A-67824/AJT).
Two copies of this sheet are enclosed.

Respectfully submitted,

Aldo J. Test, Reg. No. 18,048

FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP
 Four Embarcadero Center, Suite 3400
 San Francisco, California 94111-4187
 Telephone: (650) 494-8700 Fax: (650) 494-8771

(10/23)

2/IDS
Hawkins
6/27/00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Tang et al.

Serial No.: New

Filed: Herewith

Title: *Mass Spectrometer System Including a
Double Ion Guide Interface and Method
of Operation*

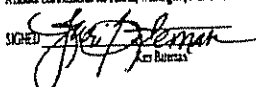
Examiner: Not assigned
Art Unit: not assigned

INFORMATION DISCLOSURE
STATEMENT

Date: December 3, 1999

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SIGNED: 
Ken Bultman

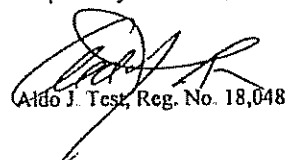
BOX DD
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicant submits herewith patents and publications which may be material to the examination of this application and in respect of which there may be a duty to disclose in accordance with 37 C.F.R. §1.56. While this Statement may be "material" pursuant to 37 C.F.R. §1.56, it is not intended to constitute an admission that any patent, publication, or other information referred to therein is "prior art" for this invention unless specifically designated as such. A listing of patents and publications is shown on enclosed Form PTO-1449 and a copy of each patent and publication is also enclosed.

This information disclosure statement is being filed in compliance with 37 CFR 1.97(b)(3) as being filed before the mailing date of the first office action on the merits. If there are any fees or credits due, authorization is given to charge or credit our Deposit Account No. 06-1300 (Order No. A-67824/AJT).

Respectfully submitted,


Aldo J. Test, Reg. No. 18,048

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